

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 01 November 2000 (01.11.00)	
International application No. PCT/US99/21049	Applicant's or agent's file reference M41.PCT
International filing date (day/month/year) 14 September 1999 (14.09.99)	Priority date (day/month/year) 16 September 1998 (16.09.98)
Applicant BHADRA, Narendra et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
12 April 2000 (12.04.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 May 2000 (22.05.00)	
International application No. PCT/US99/21049	Applicant's or agent's file reference M41.PCT
International filing date (day/month/year) 14 September 1999 (14.09.99)	Priority date (day/month/year) 16 September 1998 (16.09.98)
Applicant BHADRA, Narendra et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

12 April 2000 (12.04.00)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>F. Baechler</p> <p>Telephone No.: (41-22) 338.83.38</p>
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 07 JUN 2001

PCT

Applicant's or agent's file reference M41.PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/21049	International filing date (day/month/year) 14 SEPTEMBER 1999	Priority date (day/month/year) 16 SEPTEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61N 1/02 and US Cl.: 607/40		
Applicant AXON ENGINEERING, INC.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 13 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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Date of submission of the demand 12 APRIL 2000	Date of completion of this report 08 JANUARY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer GEORGE EVANISKO
Facsimile No. (703) 305-3230	Telephone No. (703) 308-2612

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/21049

I. Basis of the report

1. With regard to the elements of the international application: *

☒ the international application as originally filed☒ the description:

pages 1-11, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

☒ the claims:

pages 12-15, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of

☒ the drawings:

pages 1-2, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

☒ the sequence listing part of the description:

pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
☒ the claims, Nos. NONE
☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/21049

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims <u>1-10, 14</u>	YES
	Claims <u>11-13, 15-18</u>	NO
Inventive Step (IS)	Claims <u>1-10, 14</u>	YES
	Claims <u>11-13, 15-18</u>	NO
Industrial Applicability (IA)	Claims <u>1-18</u>	YES
	Claims <u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 11-13 and 15-18 lack novelty under PCT Article 33(2) as being anticipated by EP 0245547.

Claims 11-13 lack novelty under PCT Article 33(2) as being anticipated by Mortimer et al (5199430).

Claims 1-10 and 14 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method for controlling bladder discharge by coupling electrodes to the sacral ventral and dorsal roots.

----- NEW CITATIONS -----
NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference M41.PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 21049	International filing date (day/month/year) 14/09/1999	(Earliest) Priority Date (day/month/year) 16/09/1998
Applicant AXON ENGINEERING, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

1



None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/21049

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-10
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

onal Application No

PCT/US 99/21049

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 245 547 A (UNIV CALIFORNIA) 19 November 1987 (1987-11-19) page 3, line 34 -page 6, line 40 page 7, line 48 -page 11, line 39 figures	11-13, 15-18
X	US 5 199 430 A (MORTIMER J THOMAS ET AL) 6 April 1993 (1993-04-06) cited in the application the whole document	11-13
A	US 4 569 351 A (TANG PEI C) 11 February 1986 (1986-02-11) the whole document	11, 14, 15
A	US 5 370 670 A (CHANCELLOR MICHAEL B) 6 December 1994 (1994-12-06) the whole document	11, 15-18
-/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

1 February 2000

Date of mailing of the international search report

07/02/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Ferrigno, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/21049

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 3 870 051 A (BRINDLEY GILES SKEY)</p> <p>11 March 1975 (1975-03-11)</p> <p>the whole document</p> <p>-----</p>	11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/21049

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0245547 A	19-11-1987	AT 55697 T US 4607639 A	15-09-1990 26-08-1986
US 5199430 A	06-04-1993	AT 183934 T AU 1538292 A CA 2106008 A DE 69229913 D EP 0585245 A WO 9215366 A	15-09-1999 06-10-1992 12-09-1992 07-10-1999 09-03-1994 17-09-1992
US 4569351 A	11-02-1986	NONE	
US 5370670 A	06-12-1994	AU 680993 B AU 1431295 A CA 2178904 A EP 0744980 A JP 2810793 B JP 9507401 T WO 9516491 A US 5752978 A	14-08-1997 03-07-1995 22-06-1995 04-12-1996 15-10-1998 29-07-1997 22-06-1995 19-05-1998
US 3870051 A	11-03-1975	GB 1434524 A	05-05-1976

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/21049

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-10
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁷ : A61N 1/36</p>	<p>A1</p>	<p>(11) International Publication Number: WO 00/15293 (43) International Publication Date: 23 March 2000 (23.03.00)</p>
<p>(21) International Application Number: PCT/US99/21049 (22) International Filing Date: 14 September 1999 (14.09.99) (30) Priority Data: 60/100,542 16 September 1998 (16.09.98) US (71) Applicant (for all designated States except US): AXON ENGINEERING, INC. [US/US]; 15264 NEO Parkway, Garfield Heights, OH 44128 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BHADRA, Narendra [IN/US]; 2075 Coventry Road, Cleveland Heights, OH 44118 (US). MORTIMER, J., Thomas [US/US]; 13753 County Line Road, Chagrin Falls, OH 44022 (US). GRUNEWALD, Volker [DE/DE]; Konstanty-Gutschow Strasse 8, D-3000 Hannover 61 (DE). (74) Agent: LITZINGER, Jerrold, J.; Sentron Medical, Inc., Suite 600, 4445 Lake Forest Drive, Cincinnati, OH 45242 (US).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</p>
<p>(54) Title: COMBINED STIMULATION OF VENTRAL AND DORSAL SACRAL ROOTS FOR CONTROL OF BLADDER FUNCTION</p> <p>(57) Abstract</p> <p>An apparatus and technique for controlling the bladder function of a patient by combined stimulation of the ventral and dorsal sacral roots. An electrode is implanted on the sacral motor nerves while a second electrode is implanted on the sacral sensory nerves, and the nerves are stimulated using quasitrapezoidal pulse trains to selectively activate and void the bladder. The technique makes it unnecessary to perform a dorsal rhizotomy.</p> <p>small efferent - sacral motor nerves - ventral - spine to bladder large afferent - sacral sensory nerves - dorsal</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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EE	Estonia						

COMBINED STIMULATION OF VENTRAL AND DORSAL SACRAL ROOTS FOR CONTROL OF BLADDER FUNCTION

5

CROSS REFERENCE TO RELATED APPLICATIONS

This is a utility patent application taking priority from provisional patent application 60/100,524, filed September 16, 1998, which is incorporated herein by reference.

10

BACKGROUND OF THE INVENTION

15

1. Field of Invention

This invention relates generally to selective nerve stimulation for bladder control, and, in particular, to a technique by which micturition can be achieved in spinal cord injured patients without dorsal root section.

20

2. Description of the Prior Art

25

Retention of urine, leading to complications such as urinary tract infection and urinary calculi, remains a major factor leading to morbidity in spinal cord injured patients. In high cord injury, with upper motor neuron damage, the lower nerve pathways to the bladder are intact. The aim of micturition control in these individuals is to enable them to contract the bladder musculature without activating structures in the urethra that may impede urine flow. The procedure should leave an acceptable post-void residual volume within the bladder and should also be able to prevent overflow incontinence.

30

The difference in the size of the nerve fibers to the bladder or bowel and the urethral or anal sphincter allows the development of techniques to selectively activate the nerves to the bladder and bowel without the activation of the
5 sphincters.

Previously, electrical stimulation has been applied to control the bladder and bowel. The previous attempts have focused on three techniques: direct stimulation of the detrusor muscle, activation of the detrusor by stimulation of the conus
10 medullaris, and activation of the detrusor by sacral root or nerve stimulation with extensive dorsal rhizotomy. All three of these methods suffer from the same problem. They all cause contraction of the bladder to expel urine concurrently with contraction of the external urethral sphincter blocking urine flow. The rhizotomy technique also results in the loss of erection for the male. It would be advantageous
15 if contraction of the sphincter could be selectively blocked.

Techniques available for blocking nerve impulses are discussed, for example, in "A Technique for Collision Block of Peripheral Nerve: Single Stimulation Analysis", van den Honert and Mortimer, IEEE Transactions on Biomedical Engineering, Volume
20 BME-28, No. 5, May 1981, pages 373-378, and "Generation of Unidirectionally Propagated Action Potentials in a Peripheral Nerve by Brief Stimuli", van den Honert and Mortimer, Science, Volume 206, December 1979, pages 1311-1312. With the van den Honert and Mortimer techniques, a nerve impulse or action potential is generated which travels toward the brain. When the artificially generated nerve

impulse meets a motor impulse travelling from the brain, the motor impulse is collision blocked. That is, the artificially generated action potential cancels the motor action potential. If one were to apply the van den Honert and Mortimer techniques, it could be used to cause concurrent relaxation of both the bladder
5 contracting muscles and the urethral sphincter.

Sacral nerve stimulation for electrical control of bladder function has been attempted for many years; however, virtually all attempts have been plagued by problems associated with co-activation of contractile structures in the urethra that
10 impede urine flow. One such attempt is described in U.S. Patent No. 4,607,639, which issued to Tanagho, et al. This patent describes a technique in which the sacral nerves are separated to isolate the ventral and dorsal roots thereof, and the inferior somatic nerve S1 is sectioned to isolate the external sphincter on one side. The dorsal root of S2 is then sectioned unilaterally to isolate the sensory function
15 thereof. An electrode is positioned on the S3 sacral nerve to stimulate the detrusor muscles of the bladder. However, it is suggested that sphincter response may be reflexly produced using this technique, and mentions the necessity for the rhizotomy of the dorsal roots.

20 U.S. Patent No. 5, 199,430 teaches a system for selectively arresting propagation of action potentials in large diameter fibers without arresting propagation in small diameter nerve fibers using a quasitrapezoidal waveform. This waveform, which is disclosed in U.S. Patent No. 4,608,985, and its stimulation scheme made it possible to install electrodes on the sacral roots that could

differentially activate the small fibers to the detrusor and rectum without activating the large fibers to the sphincter, thus allowing bladder and bowel activation without the sphincter tone being raised. However, this procedure often involved dorsal rhizotomy to minimize any reflexogenic response.

5

The present invention contemplates a new technique for bladder function control in which a dorsal rhizotomy is unnecessary.

10

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a system and method for inducing micturition in spinal cord injured patients.

15

It is a further object of the present invention to provide a method of controlling bladder draining by stimulating nerve cuff electrodes implanted on the sacral motor roots and also the sacral sensory roots.

20

It is a still further object of the present invention to provide a method of efficiently voiding the bladder of a patient without performing a dorsal rhizotomy.

25

These and other objects are accomplished in the present invention by a method and system for selectively controlling activation of a patient's bladder by applying trains of quasitrapezoidal pulses with appropriate current amplitudes on both the ventral and dorsal sacral roots to subdue urethral reflexes and enhance voiding.

BRIEF DESCRIPTION OF THE DRAWINGS

5 FIG. 1 schematically illustrates the placement of electrodes for controlling the bladder in the present invention;

 FIG. 2 is a graphic representation showing average voided volume from different combinations of stimulus;

10

 FIG. 3 is a graphic representation showing average voided volume when combined dorsal and ventral root stimulation is used; and

 FIG. 4 illustrates a stimulation scheme which may be used for combined
15 stimulation of the dorsal and ventral roots in the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

20 Referring now to FIG. 1, there is shown an illustrative embodiment of the present invention within the environment of the human body. Kidney 10 is connected to the bladder 12 via the ureter 14, which carries away urine from kidney 10 to bladder 12. Urine is expelled from the body through bladder neck 16 and urethra 18 and out from urethral sphincter 20. Bladder 12 and sphincter 20 function
25 is controlled by action potentials traveling from spinal cord 19 primarily, but not limited to, on a pair of sacral roots 21 which consists of a segment of ventral sacral roots 22 and a segment of dorsal sacral roots 23. Dorsal roots 23 are primarily

sensory (afferent) to transmit sensation to spinal cord 19, while ventral roots 22 primarily transmit motor pulses (efferent) from spinal cord 19 to bladder 12 and sphincter 20. Although illustrated as being separated, the dorsal and ventral roots for each nerve are, in fact, normally joined together and their fibers mixed to progress as a single trunk.

Ventral roots 22 include nerve bundles 22a which include larger diameter nerve fibers and nerve bundles 22b which include smaller diameter fibers. Larger fibers 22a connect between spinal cord 19 and sphincter 20, while smaller fibers 22b connect between spinal cord 19 and bladder 12. Action potentials flowing along larger fibers 22a cause sphincter 20 to contract, blocking the outlet from urethra 18. When the bladder is to be emptied, the flow of action potentials through fibers 22a is stopped, allowing sphincter 20 to relax.

Smaller fibers 22b usually carry no action potentials until the person desires to evacuate the bladder; action potentials are then sent along fibers 22b concurrently with the stopping of action potentials along fibers 22a, causing sphincter 20 to relax and allowing bladder neck 16 to open concurrently with bladder 12 muscles contracting, thus expelling urine.

Spinal cord injuries and various other medical conditions can cause a loss of control of the bladder function. To reinstitute this control, a cuff electrode 30 can be mounted surrounding sacral ventral root 22. Cuff electrode 30, which is preferably a self-curling spiral electrode that is biased to curl around the selected root and is

described in U.S. Patent No. 4,602,624, is configured to accommodate nerves of varying diameters and can electrically excite action potentials on smaller fibers 22b while blocking naturally occurring and electrically activated action potentials from travelling downstream on larger fibers 22a. An example of this procedure is

5 described in detail in U.S. Patent No. 5, 199,430, which issued in April 6, 1993, and is hereby incorporated by reference in its entirety.

The present invention also includes an additional cuff electrode 32 which is implanted on a dorsal sacral root 23. Application of trains of quasitrapezoidal

10 pulses, which are described and taught in U.S. Patent No. 4,608,985, which patent is incorporated herein by reference, that have appropriate current amplitudes and are applied concurrently to electrodes 30 and 32 to stimulate the dorsal and ventral roots can result in the voiding of bladder contents without increasing sphincter pressures. A controller 34 is electrically coupled to electrodes 30 and 32 to provide

15 the necessary signals for this desired bladder control.

Several experiments were conducted to confirm that combined dorsal and ventral root stimulation provides an effective low pressure bladder evacuation without requiring dorsal rhizotomy.

20

EXPERIMENT 1.

Combined sensory and motor stimulus was applied to an animal under 2.5% halothane inhalation anesthesia. An efferent motor stimulus was applied by a spiral

25 nerve cuff electrode implanted on S2 motor roots. Either a quasitrapezoidal,

balanced biphasic, 20 Hz pulse, with current amplitude set at a volume determined to selectively block sphincter activity, or a conventional rectangular supra-threshold stimulus was used. The efferent sensory stimulus was applied to the S2 dermatome with surface electrodes using a 20 Hz balanced biphasic rectangular pulse at 10 to 5 15 ma. The surface stimulus was varied to be continuous or intermittent (1 second on/1 second off). The bladder was filled before each trial run with 60 ml of sterile saline.

FIG. 2 shows the average volume of fluid voided during a 10 second pulse train for each combination of stimulus trains. The results show that a combination of selective motor root activation by a quasitrapezoidal pulse train and intermittent surface stimulation to the S2 dermatome enhanced bladder emptying.

EXPERIMENT 2

15

Combined sensory and motor stimulus was applied to an animal under 2.5% halothane inhalation anesthesia. The motor stimulus was applied by a spiral nerve cuff electrode implanted on the S2 motor roots. A quasitrapezoidal, balanced biphasic, 20 Hz pulse, with current amplitude set at a value determined to selectively 20 block sphincter activity, was used. The sensory stimulus was applied to S1, S2, or S3 dermatome with surface electrodes using a 20 Hz balanced biphasic rectangular pulse at 10 to 15 ma. The intermittent surface stimulation was varied to be either 1 second on/1 second off or 0.5 seconds on/0.5 seconds off. The tests were randomized for stimulus combinations. The test results show that bladder emptying

was enhanced only when the combined sensory stimulus was applied to the S2 dermatome. The 1 second on/1 second off intermittent pattern was more effective than the 0.5 seconds on/0.5 seconds off pattern.

5 EXPERIMENT 3

Combined stimulation of the dorsal and ventral sacral roots was applied to an animal by implanting spiral nerve cuff electrodes on the sacral ventral motor roots at S2 and S3, while leaving the dorsal roots intact and implanting a spiral nerve cuff
10 electrode on one dorsal S2 root. The ventral sacral roots were stimulated with quasitrapezoidal pulse trains at 20 Hz with current amplitudes sufficient to selectively activate the bladder or with 20 Hz conventional rectangular pulses. At the same time, a 20 Hz intermittent stimulus, 1 second on/ 1 second off was applied to the S2 dorsal root.

15

Table 1 shows the average results from three trials for each stimulus pattern. For 10 seconds of motor stimulation, an average increase of 66% in flow rate was observed during combined motor and sensory stimulation, while FIG. 3 shows the average volumes voided.

20

TABLE 1

Pulse Type	Qmax	V(ml)	Pv (Qmax)	Pu (Qmax)	Pv max	Pu max
20 Hz R	2.3	6.0	50.0	40.0	117.5	160.0
20 Hz Q	2.4	7.0	78.8	57.5	111.3	99.4
Aff + 20 Hz Q	4.0	27.0	59.2	51.7	85.0	80.0

Q_{max} = Average maximum flow rate in ml/sec
 $V(ml)$ = Average voided volume in ml
 $P_v(Q_{max})$ = Maximum bladder pressure in cm of water at maximum flow
5 $P_u(Q_{max})$ = Average sphincter pressure in cm of water at maximum flow
 $P_v \text{ max}$ = Maximum bladder pressure in cm of water
 $P_u \text{ max}$ = Maximum sphincter pressure in cm of water

10 FIG. 4 illustrates the stimulus pattern for the combined dorsal and ventral root stimulation of the present invention. An intermittent pulse train 100 is applied to dorsal root 23 via cuff electrode 32, while a continuous pulse train 102 is simultaneously applied to ventral root 22 via cuff electrode 30. In this manner, low pressure bladder activation can be achieved by modulating the reflexes associated

15 with the neural system for micturition control and eliminate the need for dorsal rhizotomies.

Pulse train 100 preferably consists of pulses delivered at a frequency of 10 to 35 Hz, with each pulse having a nominal amplitude of less than 1 ma and a pulse

20 duration of 10 to 100 μsec . Pulse train 100 is generated intermittently, with a pattern of 0.25 to 1 second on/ 0.25 to 1 second off. Pulse train 102 preferably consists of a continuous series of quasitrapezoidal pulses of 350 to 500 μsec duration and a nominal amplitude of 1 ma delivered at a frequency of 15 to 30 Hz.

25 While the invention has been shown and described in terms of several preferred embodiments, it will be understood that this invention is not limited to

these particular embodiments and that many changes and modifications may be made without departing from the true spirit and scope of the invention as defined in the appended claims.

WHAT IS CLAIMED IS:

1. A method for controlling bladder discharge in a patient, comprising the steps
5 of:

coupling a first electrode to a sacral ventral root of said patient;

- coupling a second electrode to a sacral dorsal root corresponding to
10 said ventral root of said patient;

and transmitting a series of stimulus pulses to said first and second
electrodes simultaneously to cause discharge of the bladder

- 15 2. The method of claim 1 wherein said first electrode comprises a self-sizing cuff
electrode.

3. The method of claim 1 wherein said second electrode comprises a self-sizing
cuff electrode.

- 20 4. The method of claim 1 wherein said second electrode comprises a surface
electrode.

5. The method of claim 1 wherein said stimulus pulses transmitted to said first
25 electrode comprise a quasitrapezoidal pulse train at 20 Hz.

6. The method of claim 1 wherein said stimulus pulses transmitted to said first electrode comprise a conventional rectangular pulse train at 20 Hz.
7. The method of claim 1 wherein said stimulus pulses transmitted to said
5 second electrode comprise an intermittent pulse train at 20 Hz having a one second on/ 1 second off pattern.
8. The method of claim 1 wherein said first and second electrodes are applied to the dorsal and ventral roots of the S3 sacral nerve.
- 10 9. The method of claim 1 wherein said stimulus pulses transmitted to said second electrode have a nominal amplitude of less than 1 ma and a pulse duration of 10 to 100 μ sec.
- 15 10. The method of claim 1 wherein said stimulus pulses transmitted to said first electrode have a nominal amplitude of 1 ma and a pulse duration of 350 to 500 μ sec.
11. An apparatus for the control of bladder function in a patient by combined
20 stimulation of ventral and dorsal sacral roots, said apparatus comprising:

a first electrode, applied to a ventral sacral root of a patient;

a second electrode, applied to a dorsal sacral root corresponding to
25 said ventral sacral root;

and control means, electrically coupled to said first and second electrodes, for generating a series of stimulus pulses simultaneously to said first and second electrodes sufficient to cause the bladder of said patient to contract, whereby emptying said bladder.

12. The apparatus of claim 11, wherein said first electrode comprises a self-sizing cuff electrode.

10 13. The apparatus of claim 11, wherein said second electrode comprises a self-sizing cuff electrode.

14. The apparatus of claim 11, wherein said second electrode comprises a surface mounted electrode.

15 15. The apparatus of claim 11, wherein said stimulus pulses generated to said first electrode by said control means comprises a quasitrapezoidal pulse train at 20 Hz.

20 16. The apparatus of claim 11, wherein said stimulus pulses generated to said second electrode by said control means comprise an intermittent pulse train pattern of 1 second off/ 1 second on.

17. The apparatus of claim 11, wherein said stimulus pulses generated to said first electrode by said control means have a nominal amplitude of 1 ma and a pulse duration of 350 to 500 μ sec.
- 5 18. The apparatus of claim 11, wherein said stimulus pulses generated to said second electrode by said control means have a nominal amplitude of less than 1 ma and a pulse duration of 10 to 100 μ sec.

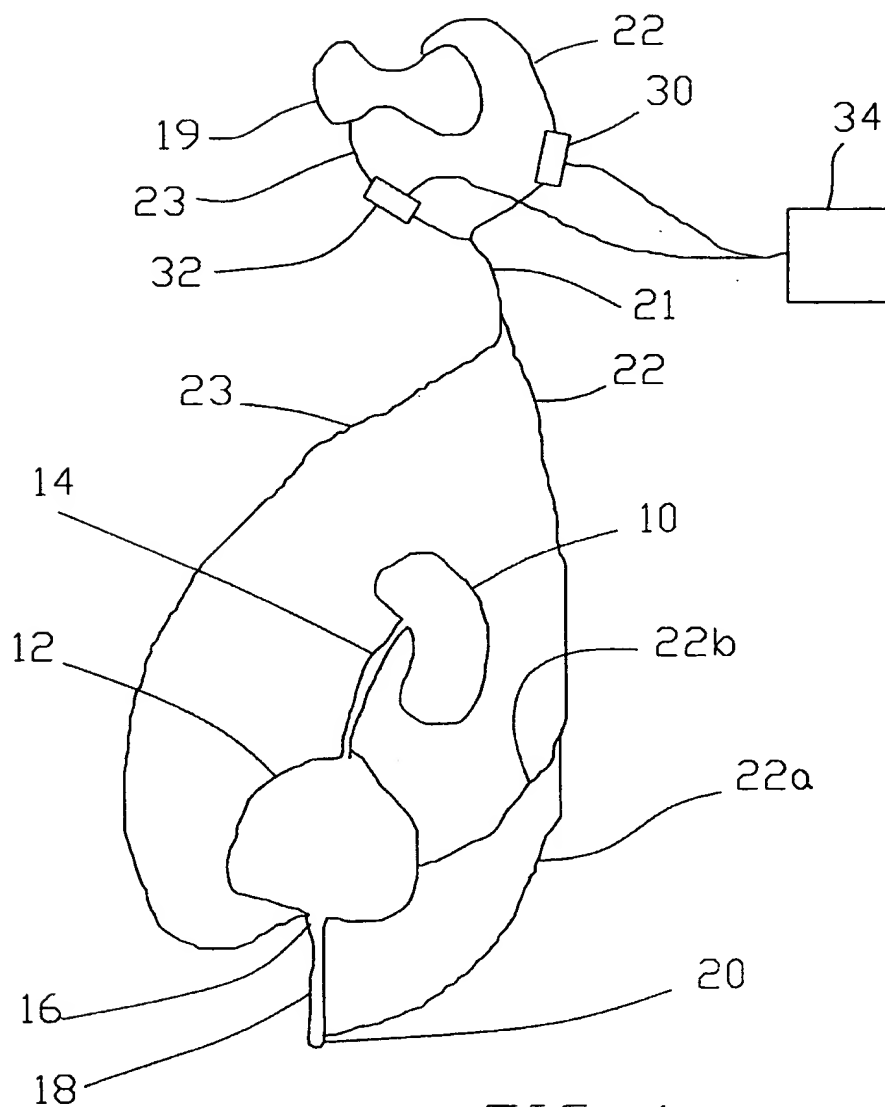


FIG. 1

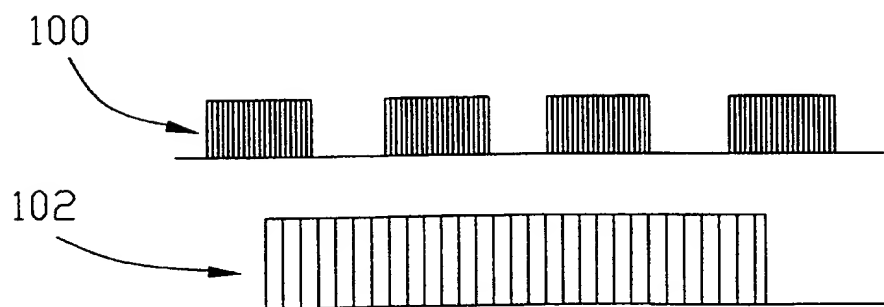
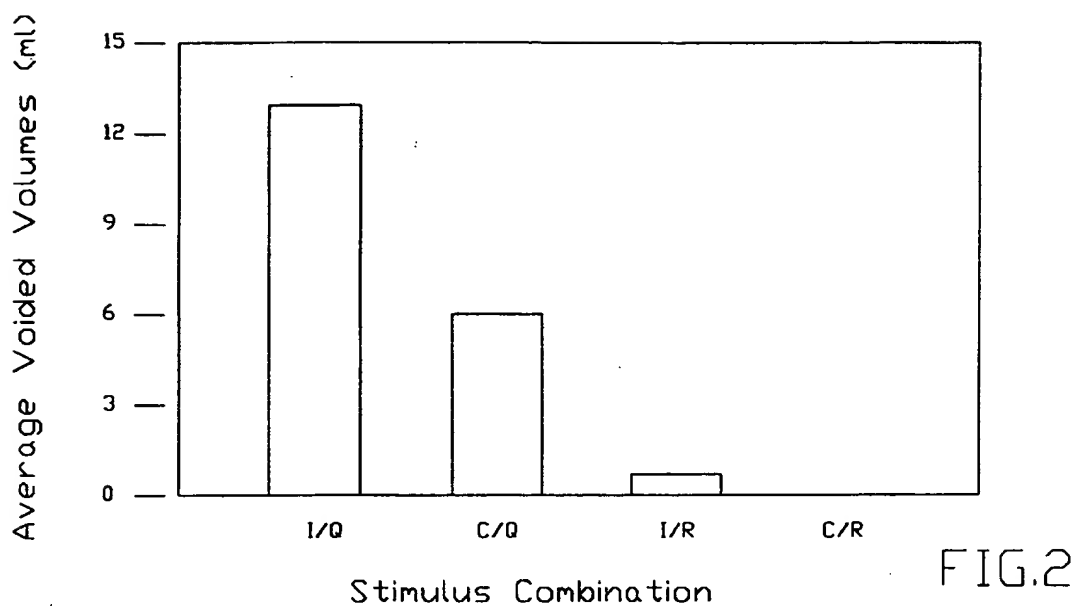


FIG. 4



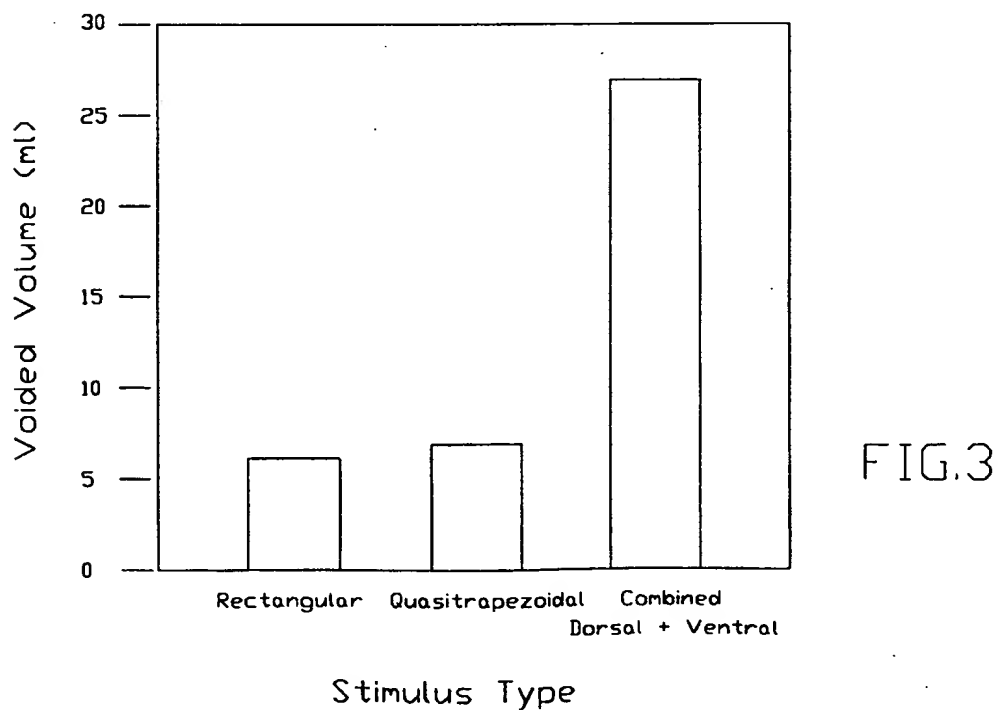
Average Voided Volumes During a 10 Second Pulse Train

I/Q = Intermittent surface stimulation with Quasitrapezoidal motor pulses

C/Q = Continuous surface stimulation with Quasitrapezoidal motor pulses

I/R = Intermittent surface stimulation with Rectangular motor pulses

C/R = Continuous surface stimulation with rectangular motor pulses



INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/21049

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 245 547 A (UNIV CALIFORNIA) 19 November 1987 (1987-11-19) page 3, line 34 -page 6, line 40 page 7, line 48 -page 11, line 39 figures	11-13, 15-18
X	US 5 199 430 A (MORTIMER J THOMAS ET AL) 6 April 1993 (1993-04-06) cited in the application the whole document	11-13
A	US 4 569 351 A (TANG PEI C) 11 February 1986 (1986-02-11) the whole document	11,14,15
A	US 5 370 670 A (CHANCELLOR MICHAEL B) 6 December 1994 (1994-12-06) the whole document	11,15-18
-/-		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

1 February 2000

Date of mailing of the international search report

07/02/2000

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INTERNATIONAL SEARCH REPORT

Inter national Application No
PCT/US 99/21049

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 870 051 A (BRINDLEY GILES SKEY) 11 March 1975 (1975-03-11) the whole document -----	11

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/21049

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-10
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/21049

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